B1 conclude

A_3 is described in EP 0259780. All the above mentioned patents are incorporated herein by reference.

Please replace the paragraph from page 1, line 28 through page 2, line 2, with the following:

B2

The structure of ramoplanin and its factors and derivatives have been described in several articles and publications, see R. Ciabatti et al., J. Antib. 1989, 254-267, J. K. Kettenring et al., J. Antob 1989, 268-275, R. Ciabatti and B. Cavalleri, Bioactive Metabolites from Microorganisms, Elsevier Science Publishers, 1989, 205-219 and M. Kurz and W. Guba, Biochemistry 1996, 35, 12570-12575.

Please replace the paragraph at page 3, lines 9-10 as follows:

R' represents alpha-D-mannopyranosyl or s-o-alpha-D-mannopyranosyl-alpha-D-mannopyranosyl,

Please replace the paragraph at page 6, lines 15-24 as follows:

B3

Typically, a fat emulsion product suitable for preparing a formulation of the invention comprises an oil phase (usually 2-40%, preferably, 5-25% weight/vol), preferably consisting of vegetable oils such as soybean oil, safflower oil and cottonseed oil, emulsifiers (usually 0.2-5%, preferably, 0.5-2% weight/vol), preferably based on phospholipids of egg source such as egg lecithin or soybean lecithin, and additives as osmotic agents such as glycerol, sorbitol and xylitol.

Please replace the paragraph from page 6, line 26 through page 7, line 2 as follows:

B4

These fat emulsion products, as commercially available, are emulsions comprising the above mentioned oil phase, emulsifiers and additives dispersed in water for injection and the oil phase is generally present in the emulsion in a percentage (weight/vol) of 5 to 25%. For preparing the i.v. administrable formulation of this invention, the fat emulsion product may

B4 Conclude be used as such or diluted with saline or water for injection added with an osmotic agent (e.g. glucose) to decrease the oil phase concentration to a lower value and, at the same time, maintaining the desired osmolarity.

Please replace the paragraph on page 7, lines 8-15 as follows:

B5 For instance, with ramoplanin concentrations of about 10 mg/ml, the percentage of the oil phase in the i.v. formulations of the invention may range between 4 to 40% (weight/vol) although are preferred those i.v. fat emulsions wherein the oil phase is between 4 and 25%, and, more preferably, between 8 and 18%, with the range 8-10% being currently the most preferred concentration.

Please replace the paragraph at page 11, lines 27-33 as follows:

B6 The results of a first set of tolerability studies of representative examples of formulations of the invention in rats at a concentration of ramoplanin of 10 mg/ml (dose 20 mg/kg, administration volume 2 ml/kg), in comparison with a conventional i.v. formulation of the same active principle, are summarized in the following.

Please replace the paragraph on page 12, lines 1-18 as follows:

B7 More particularly, ramoplanin in a conventional aqueous vehicle (0.9% saline) or in the formulations of the invention wherein the proportion of the oil phase in the total formulation is between 2 and 8% (weight/vol) is administered to rats (3-5 animal/group) at a dose of 20 mg/kg (drug concentration 10 mg/ml). The administered volume is 2 ml/kg, according to the animal weight on the day of administration, and the injection speed is 0.1 ml/sec. The intravenous administration is into the caudal vein. Treatments are planned for three days at 24 hours intervals. Control rats receive either 0.9% saline or an equivalent volume of Intralipid® 10%. Behavior and physical appearance are observed frequently the day of dosing. Urine appearance is also recording within 3 h after each daily treatment. Rats

B7 are sacrificed 24 h after the last treatment. The results of these experiments are summarized in Table II.

On page 13, please replace the caption for Table II to read as follows:

B8 **Table II.** Urine appearance, gross pathology at the injection site and clinical observations of rats treated with ramoplanin formulated with Intralipid® or in a conventional aqueous vehicle (0.9% saline)

Please replace the paragraph on page 14, lines 20-33 as follows:

B9 A second set of experiments was carried out to determine tolerability of the formulation of the invention according to the same procedure described above but administering a dose corresponding to 10 mg/kg instead of 20 mg/kg to several groups of three rats for 3 days at 24 hours intervals. The concentration of ramoplanin in the formulation was 1 mg/ml instead of 10 mg/ml and the volume of the formulation administered to each rat was 10 ml/kg instead of 2 ml/kg. The Intralipid® fat emulsion product was added in several different proportion as represented in the following Table III where the same parameters considered in Table II are reported. The rats were killed 24 h after the last treatment.

On page 15, please replace the caption of Table III to read as follows:

B10 **Table III.** Urine appearance, gross pathology at the injection site and clinical observations of rats treated with ramoplanin formulated with Intralipid® or in a conventional aqueous vehicle (0.9% saline)

Please replace the paragraph on page 17, lines 12-16 as follows:

B11 When the gentamicin or vancomycin are employed as comparators, they are administered subcutaneously and second shot is given 5 h after infection. Rifampicin and teicoplanin are administered subcutaneously in single dose 10 min after infection.